

Intarcia Dkt No. ALE 053.16  
 USSN: 10/645,293  
 PATENT

# Remarks

## **I. Addressing The Examiner's Rejections.**

### **1. Rejection of Claims 54 and 70 under 35 U.S.C. §112, First Paragraph.**

The Examiner rejected claims 54 and 70 under 35 U.S.C. §112, first paragraph, asserting that they fail to comply with the written description requirement. The Examiner further asserted that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that the claims recite "the reservoir comprises a metal capsule" and that the specification contains no support for a "metal capsule."

The specification describes that suitable materials for reservoirs for the implantable devices of the present invention include non-reactive polymers or biocompatible metals or alloys (*see, e.g.*, Specification, page 8, line 18, to page 9, line 24). The term capsule was used to refer to an exemplary physical structure of the reservoir, for example, 12 of Figure 2. In order to expedite prosecution, the term "capsule" is removed from claim 54. Claim 70 is canceled by this amendment.

In view of applicants' amendment and arguments, applicants submit that the rejection of the claims under 35 U.S.C. §112, first paragraph, has been overcome. Applicants respectfully request withdrawal of the rejection.

### **2. Rejection of Claims 51-73 and 75 Under 35 U.S.C. §103(a).**

The Examiner rejected claims 51-73 and 75 under 35 U.S.C. 103(a) asserting that the claims are unpatentable over Laby, et al., U.S. Patent No. 4,623,330 in view of Portner, et al., U.S. Patent No. 4,360,019, Magruder, et al., U.S. Patent No. 5,238,687, and further in view of Mia, U.S. Patent No. 5,519,002.

To reject a claim based on combining prior art elements according to known methods to yield predictable results, the Examiner must resolve the Graham factual inquiries. *See Graham v. John Deere Co.*, 383 USC 1, 86 S. Ct. 684, 15 L Ed2d 545, 148 USPQ 459, S. C. 1966. The Examiner must then articulate the following: (1) a finding that the prior art includes each element claimed with the only difference between the claimed invention and the prior art being the lack of actual combination of the elements in a single prior art

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reference; (2) a finding that one of ordinary skill in the art could have combined the elements as claimed by known methods and that in combination each element merely would have performed the same function as it did separately; (3) a finding that one of ordinary skill in the art would have recognized that the results of the combination were predictable; and (4) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. (See Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* 57526, 57529 Federal Register / Vol. 72, No. 195.)

The cited references do not teach all of the elements of the independent claims as presented in the accompanying amended claim set. Accordingly, a case of *prima facie* obviousness cannot be established.

The pending independent claims each contain a limitation related to (i) the reservoir and back diffusion regulating outlet having surfaces in a mating relationship wherein a helical flow path is formed between the mating surfaces (*see* claims 51, 52 and 71), or (ii) an exterior surface of the semipermeable plug includes circumferential ridges (*see* claims 55 and 61).

First, none of the cited references teaches the reservoir and back diffusion regulating outlet having surfaces in a mating relationship wherein a helical flow path is formed between the mating surfaces. The reference of Laby, et al., teaches only an open end 43 and a nozzle portion 44 to receive a hypodermic needle (*see, e.g.,* Laby, et al., col. 5, lines 14-25). The reference of Portner, et al., teaches only "The housing 22 also includes internal structure forming a plurality of outlet chambers providing serial communication between the appendage 42 of the pumping chamber 28 and the catheter 15. The outlet chambers are indicated in FIG. 3, respectively at 44 and 46, the outlet chamber 46 being a final chamber which is in direct communication with the catheter 15" (*see* Portner, et al., col. 4, lines 63-66; emphasis added). Magruder, et al., teaches only a "passageway, orifice, or the like, through first wall section 12a for communicating with compartment 18. The expression 'at least one passageway' includes aperture, orifice, bore, pore, porous element through which the agent can migrate, hollow fiber, capillary tube, porous overlay, porous insert, and the like" (*see* Magruder, et al., col. 11, lines 58-64). There are no teachings in the reference of Mia

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concerning a flow path.

In the Office action, mailed 27 March 2008, the Examiner notes that "Laby fails to disclose the helical path flow that regulates the back diffusion through the outlet" (*see* Office action, mailed 27 March 2008, page 4). The Examiner attempts to combine the teachings of Portner, et al., with the primary reference by stating "It would have been obvious to one of ordinary skills in the art to us [*sic*] a spring as a valve at the outlet of drug implantable system to regulate the drug release and prevent the back diffusion of the external fluids because portner [*sic*] teaches that the drug can be prevented from flowing back" (*see* Office action, mailed 27 March 2008, page 5). However, the spring-related teachings of Portner, et al., do not provide the required teaching of the reservoir and back diffusion regulating outlet having surfaces in a mating relationship wherein a helical flow path is formed between the mating surfaces.

Further, the Examiner's statements that "it would have been obvious" are merely conclusionary statements unsupported by any teaching or suggestion in the cited art. No evidence has been provided by the Examiner to support these conclusions.

Second, none of the cited references teaches a water-swellaable semipermeable plug that is received in sealing relationship with an interior of the surface of an open end of an implantable reservoir the exterior surface of the semipermeable plug including circumferential ridges. The reference of Laby, et al., only teaches gas permeable membranes, not water-swellaable membranes for use in a fluid environment. As stated by Laby, et al., "[t]he present invention now proposes limitation of the operation of a spring driven device totally to gas diffusion by using a gas-tight plunger and a gas diffusion membrane in the wall of the device connecting the spring chamber with the external environment" (*see* Laby, et al., col. 1, lines 51-56). The reference of Portner, et al., contains only one teaching related to semipermeable membranes and that one teaches away from the presently claimed invention (*see* discussion below). The reference of Magruder, et al., teaches only "a second wall section that permits the passage of fluid into the delivery device, i.e. is fluid-permeable" (*see, e.g.,* Abstract, and col. 5, lines 21-41). wherein the second wall section is a section of the wall of the delivery device. There are no teachings in the reference of Mia regarding membranes.

In the Office action, the Examiner asserts "[i]t would have been obvious to one of

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ordinary skill in the art to upgrade the membranes disclosed by Portner and use a semipermeable membranes as it restricts the passage of fluid into the delivery device, i.e. is substantially fluid-impermeable." The Examiner's statement that "it would have been obvious" is merely a conclusionary statement unsupported by any teaching or suggestion in the cited art. No evidence has been provided by the Examiner to support this conclusion. Further, it is unclear why the Examiner states that use of a semipermeable membrane restricts the passage of fluid into the delivery device, i.e., it is substantially fluid impermeable. This statement is incorrect in regard to the present invention. The semipermeable membranes of the present invention are water-swellaable membranes that allow the imbibition of fluid into the claimed device (*see, e.g.*, Specification, page 9, line 25, to page 10, line 9). Clarification of the Examiner's statement is respectfully requested.

As noted above, the teachings of the reference of Portner, et al., teach away from the presently claimed invention as illustrated by the following quotation from the Background section of the reference:

Certainly drug delivery systems have been considered for complete implantation within the body of a patient. Possibly, the most common type of device employed in this manner in the prior art has included a permeable membrane for controlled diffusion of a drug into the body from a suitable reservoir. However, such devices are limited in application primarily since the rate at which the drug is delivered to the body is completely dependent upon the rate of diffusion through the permeable membrane. Once the device is implanted within the body, external control over the device is no longer possible. Accordingly, the rate of drug delivery to the body may be affected by differing conditions within the body. In addition, such systems make no provisions for the adjustment of the rate or time interval for drug delivery, nor can the delivery rate be easily varied. (*See Portner, et al., col. 1, lines 32-48, emphasis added*).

The Examiner has provided no reasoning or evidence that would lead one of ordinary skill in the art to modify the teachings of Portner, et al., with the teachings of Magruder, et al. In fact, such a modification of the reference of Portner, et al., suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicants because the reference of Portner, et al., teaches the infusion device disclosed therein is different from and has advantages over devices using controlled diffusion membranes. The Federal Circuit held the following in *In re Gurley*, 27 F.3d 551, 553, 31

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USPQ 2d 1130, 1131 (Fed. Cir. 1994):

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant. *See United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966) ("known disadvantages in old devices which would naturally discourage the search for new inventions may be taken into account in determining obviousness").

The dependent claims distinguish over the combination of references by virtue of their incorporation of the limitations of the independent claim from which they depend.

Accordingly, applicants submit that the Examiner has failed to establish a case of *prima facie* obviousness for the presently claimed invention as none of the cited references teaches the elements of the claimed invention. In view of the above-presented arguments, applicants respectfully request that the rejection under 35 U.S.C. §103 be withdrawn.

**(2) The Primary and Secondary References Teach Away From the Claimed Invention.**

Even if, *in arguendo*, the elements of the invention were taught by the prior art, obviousness cannot be established if the prior art teaches away from the claimed invention. The Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* (57526, at 57529 Federal Register / Vol. 72, No. 195) state the following:

"Note that combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art." (Regarding "teaching away" the guidelines cite, *United States v. Adams*, 383 U.S. 39, 51-52, 148 USPQ 479, 483 (1966), wherein the Supreme Court would not require that one of ordinary skill in the art ignore the teaching away of the prior art.).

The primary reference of Laby, et al., teaches the following:

Our earlier application also makes reference to the limitation of capsule operation by diffusion of gas through the core of matrix, past the loose-fitting plunger, into the spring chamber. The present invention now proposes limitation of the operation of a spring driven device totally to gas diffusion by

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using a gas-tight plunger and a gas diffusion membrane in the wall of the device connecting the spring chamber with the external environment. (*See* Laby, et al., col. 1, lines 47-56.)

Thus the invention of the reference of Laby, et al., is limited to the "improvement" of the total operation of a spring driven device by gas diffusion. The present invention is directed to a fluid-imbibing device for delivering an active agent to a fluid environment of use. The limitation of a device operated totally by gas diffusion is inapplicable to the devices of the present invention.

As discussed herein above, the secondary reference of Portner, et al., teaches an implantable diffusion device that is alleged to overcome shortcomings of implantable devices having permeable membranes that provide controlled diffusion of a drug into the body from a reservoir (*see* Portner, et al., Background, col. 1, lines 32-65). In particular, the reference of Portner, et al., criticizes controlled diffusion devices, for example, as follows: "However, such devices are limited in application primarily since the rate at which the drug is delivered to the body is completely dependent upon the rate of diffusion through the permeable membrane" (*see* Portner, et al., col. 1, lines 37-41).

The devices of the present invention rely on the uptake of fluids through the semipermeable membrane in order to effect a steady-state release of active agent (*see, e.g.*, Specification, page 9, line 31, to page 10, line 5). Accordingly, the reference of Portner, et al., explicitly teaches away from the present invention.

A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered. *See, e.g., Bausch & Lomb v. Barnes-Hind/Hydrocurve*, 796 F.2d 443, 230 USPQ 416 (CAFC 1986). Prior art may be considered not to teach an invention, and thereby fail to support an obviousness rejection, when the stated objectives of the prior art reinforce such an interpretation. *See, e.g., WMS Gaming Inc. v. International Game Tech*, 184 F.3d 1339, 51 USPQ2d 1385, 1400 (Fed. Cir. 1999). In the present situation, the stated objective of the reference of Laby, et al., is to the operation of a spring driven device totally by gas diffusion. The stated objective of the reference of Portner, et al., is to provide an improved implantable diffusion device that overcomes the shortcomings of, for example, previously described drug delivery systems that rely on controlled diffusion. Accordingly, the references of Laby, et al., and Portner, et al., teach

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away from the fluid-imbibing devices of the present invention. Applicants submit that modification of the references to achieve a contrary purpose to the stated objectives of the references is inappropriate and does not support a conclusion of obviousness. None of the cited secondary references makes up for these shortcomings of the references of Laby, et al., and Portner, et al.

The dependent claims distinguish over the combination of references by virtue of their incorporation of the limitations of the independent claim from which they depend.

Accordingly, applicants submit that the Examiner has failed to establish a case of *prima facie* obviousness for the presently claimed invention as modification of the cited references along the lines suggested by the Examiner is counter to the stated intention of the reference. In view of the above-presented arguments, applicants respectfully request that the rejection under 35 U.S.C. §103 be withdrawn.

### (3) Secondary Considerations.

In *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727; 167 L. Ed. 2d 705; 2007 U.S. LEXIS 4745; 75 U.S.L.W. 4289; 82 USPQ.2D 1385 (S.Ct. 2007), the Supreme Court reaffirmed use of the Graham factors in the determination of obviousness under 35 U.S.C. §103(a). The four factual inquiries under Graham are: (a) determining the scope and contents of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary consideration. See *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 86 S. Ct. 684, 15 L. Ed. 2d 545, 148 USPQ 459, 467 (S.Ct. 1966).

None of the cited references presents any data that demonstrate the usefulness or efficacy of the claimed back-diffusion regulating outlet of the present invention, wherein the outlet is a helical flow path formed between the mating surfaces of the reservoir and the back diffusion regulating outlet. The present specification, on the other hand, illustrates the efficacy of the back-diffusion regulating outlet and advantages of its use, for example, preventing back-diffusion of external fluid into the active agent formulation within the reservoir, preventing back-pressure build-up in the device, and providing a release rate of active agent governed by the osmotic pumping rate (*see, e.g.*, Specification, page 6, line 24, to page 7, line 21).

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Further, the present specification teaches advantages of the water-swellaible semipermeable plug that is received in sealing relationship with an interior of the surface of an open end of an implantable reservoir, the exterior surface of the semipermeable plug including circumferential ridges. Such advantages include the following: (i) that the semipermeable plug is resiliently engaged with the interior surface of the reservoir wherein the circumferential ridges serve to frictionally engage the semipermeable plug with the interior of reservoir; (ii) the ridges serve to produce redundant circumferential seals that function before the semipermeable plug expands due to hydration; and (iii) the clearance between the ridges and the interior surface of the reservoir prevents hydration swelling from exerting stresses on the reservoir that can result in tensile failure of the reservoir or compression or shear failure of the plug (*see, e.g.,* Specification, page 7, line 22, to page 8, line 10).

Accordingly, these unappreciated and unexpected advantages of the present invention should be evaluated in the context of any asserted rejection under 35 U.S.C. §103(a). Applicants submit that the Examiner has not addressed these secondary considerations and respectfully requests their consideration.

**(4) The Examiner's Arguments.**

In the Office action, mailed 27 March 2008, the Examiner asserted the following:

It would have been obvious to an ordinary skilled man in the art to adjust these dimensions according to the human body. (Office action, mailed 27 March 2008, page 4).

The device taught by the reference of Laby, et al., is intended for intra-ruminal or intra-vaginal use (*see* Laby, et al., col. 1, lines 12-22). There is no teaching or suggestion in the cited references that would support the Examiner's assertion that the dimensions of the device of Laby, et al., (i.e., 10 ml to 50 ml syringes) could possibly be sized for use as an implantable device (e.g., subcutaneous implantation – *see* Specification, page 18, lines 13-26). The Examiner has presented no evidence or reasoning to support this assertion.

In the Office action, mailed 27 March 2008, the Examiner asserted the following:

Portner teaches that the reservoir (12) and the regulator (13) are in mating relation and the flow path (34) is between the mating surfaces (*see* Fig. 2). (Office action, mailed 27 March 2008, page 7.)

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This assertion is incorrect. First, the reference of Portner, et al., does not even teach a helical flow path. The illustration of the “tube 34 that communicates with an appendage 42 of the pumping chamber portion” (*see* Portner, et al., col. 4, lines 38-40) is not even a helical tube. Most importantly, the reservoir chamber portion 26 (not 12 of Fig. 2) does not create a flow path between “mating surfaces” with the implanted power and control system 13 (*see* Portner, et al., col. 1, lines 33-38, and col. 4, lines 20-66). In fact, prevention of insulin flowing back into the reservoir is controlled by a valve 41 and the flow path is not a helical flow path, rather the flow path is “plurality of outlet chambers providing serial communication between the appendage 42 of the pumping chamber 28 and the catheter 15.

In the Office action, mailed 27 March 2008, the Examiner also asserts that “the instant claims renders obvious over the combination of Laby, Portner, Magruder, and Mia” (Office action, mailed 27 March 2008, page 8). It is unclear to applicants why the Examiner states that the “instant claims” render anything obvious. Prior art should be applied to the claims not vice versa. Clarification is requested. The Examiner’s assertion that the “circumferential sleeve” of the reference of Magruder, et al., used to modify the teachings of the references of Laby, et al., and Portner, et al., would meet the elements of the presently claimed invention is unsupported by any reasoning or evidence in the cited references. As noted above, none of the cited references teaches a semipermeable plug with circumferential ridges. A circumferential sleeve surrounding a wall section permeable to the passage of fluids is not equivalent or suggestive of a semipermeable plug with circumferential ridges. Applicants respectfully request that the Examiner clarify the basis of the rejection pointing to specific teachings of the references by column and line numbers.

## II. Request for Telephonic Interview.

Before issuance of the next Office action, applicants respectfully request an interview with the Examiner and the Examiner’s supervisor (Michael G. Hartley, SPE, Art Unit 1618). Applicants’ representative will contact the Examiner to schedule the interview within six weeks after submission of this paper. If the Examiner takes up this application for further action before that time, the Examiner is respectfully requested to contact the undersigned so that an interview can be timely scheduled.

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**III. Conclusion.**

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. § 112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

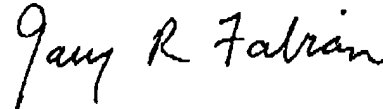
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If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 780-9030.

Respectfully submitted,



Dated: 29 September 2008

By :

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